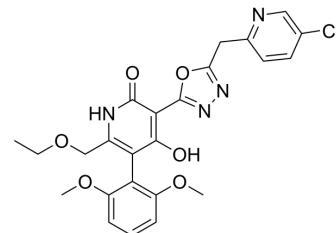


BMS-986224

| | | | |
|--------------------|------------------------|----------|---------|
| Cat. No.: | HY-139485 | | |
| CAS No.: | 2055200-88-7 | | |
| Molecular Formula: | $C_{24}H_{23}ClN_4O_6$ | | |
| Molecular Weight: | 498.92 | | |
| Target: | Apelin Receptor (APJ) | | |
| Pathway: | GPCR/G Protein | | |
| Storage: | Powder | -20°C | 3 years |
| | | 4°C | 2 years |
| In solvent | -80°C | 6 months | |
| | -20°C | 1 month | |



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20.83 mg/mL (41.75 mM; ultrasonic and warming and heat to 60°C)

| Preparing Stock Solutions | Concentration | Solvent Mass | | |
|---------------------------|---------------|--------------|------------|------------|
| | | 1 mg | 5 mg | 10 mg |
| | 1 mM | 2.0043 mL | 10.0216 mL | 20.0433 mL |
| | 5 mM | 0.4009 mL | 2.0043 mL | 4.0087 mL |
| | 10 mM | 0.2004 mL | 1.0022 mL | 2.0043 mL |

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: $\geq 2.08 \text{ mg/mL}$ (4.17 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: $\geq 2.08 \text{ mg/mL}$ (4.17 mM); Clear solution

BIOLOGICAL ACTIVITY

| | |
|---------------------------|--|
| Description | BMS-986224 is a potent, selective and orally active APJ receptor agonist ($K_d = 0.3 \text{ nM}$). BMS-986224 exhibits similar receptor binding and signaling profile to (Pyr ¹) apelin-13. BMS-986224 has the potential for the research of heart failure ^[1] . |
| IC ₅₀ & Target | Kd: 0.3 nM (APJ receptor) ^[1] |
| In Vitro | BMS-986224 fully inhibits forskolin-mediated cAMP production, with an EC ₅₀ for human APJ of 0.02 nM. BMS-986224 (0-100 nM) fully stimulates β -arrestin recruitment, ERK phosphorylation, and APJ internalization in Chinese hamster ovary-K1 or HEK293 ZF cells ^[1] . BMS-986224 is a potent and selective APJ receptor agonist that exhibits a similar signaling profile to (Pyr1) apelin-13 ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

In Vivo

BMS-986224 (0.192 mg/kg or 3 mg/kg; SC infusion; daily;) in the RHR model increased stroke volume and cardiac output to levels seen in healthy animals but without preventing cardiac hypertrophy and fibrosis, effects differentiated from enalapril [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|-----------------|--|
| Animal Model: | Male Sprague-Dawley rats (renal hypertensive rat model) ^[1] |
| Dosage: | 0.192 mg/kg or 3 mg/kg |
| Administration: | SC infusion; daily; Initiated 3 days before surgery and continued for 7 days after surgery |
| Result: | The achieved steady-state plasma concentrations during 10-day infusion were 102 and 2686 nmol/L at low dose and HD, respectively. At the low dose, BMS-986224 increased SV and CO without affecting other measured parameters, including the measured diastolic parameters, cardiac fibrosis, and heart weight in RHR. |

REFERENCES

- [1]. Gargalovic P, et al. In Vitro and In Vivo Evaluation of a Small-Molecule APJ (Apelin Receptor) Agonist, BMS-986224, as a Potential Treatment for Heart Failure. *Circ Heart Fail.* 2021;14(3):e007351.

Caution: Product has not been fully validated for medical applications. For research use only.

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